

**REMARKS**

Applicants thank the Examiner for her suggestions regarding the conditions for receiving the benefit of the filing date of the earlier filed provisional application no. 60/301,429 filed June 29, 2001. Accordingly, applicants submit herewith an amendment to the specification inserting a specific reference to this prior application in the first sentence of the specification.

Additionally, applicants thank the Examiner for her suggestions regarding the drawings. Accordingly, applicants submit herewith drawing Figs. 1-6 for inclusion in the present application. These drawings are identical to those presented in the provisional application no. 60/301,429 to which the present application claims priority. Further, these drawings are sufficiently described in the instant application so as not to represent the addition of new matter, as follows:

**Fig. 1:** Paragraph 45 on page 18 discloses that Fig. 1 shows a pedigree of Dutch autosomal dominant hemochromatosis family with haplotypes for chromosome 2q markers (ordered from centromere to telomere). The representations of the black, white, and partly filled symbols are described, as is the "+" identifier. Further, the bars next to haplotypes are described as indicating a shared risk haplotype.

Paragraph 54 and Table 1 on page 21 further provide support for Fig. 1. These passages describe the Dutch

family having hemochromatosis segregates as a dominant trait studied in Fig. 1. Lod scores were reported for several markers on chromosome 2q in the family.

Pages 22-24 of the application as filed additionally provide support for Fig. 1. These pages provide a description of symptoms exhibited by patients having hemochromatosis, findings aided by the results of the study presented in Fig. 1. In particular, paragraph 58 presents a specific summary of data shown in Fig. 1.

**Fig. 2:** Paragraph 46 on page 18 discloses that Fig. 2 shows the genomic structure of FPN1 spanning 20 kb. The representations for exons (including number and size, introns, flanking polymorphic markers, and the 5' and 3' untranslated regions are disclosed. An iron responsive element is disclosed as located in the 5' region of exon 1. This paragraph further discloses that the A-to-C transversion at the (A734) or (A430C) positions leading to an asparagine substitution by histadine at position 144 (N144H) is indicated by an arrow.

Paragraph 60 on page 24 further provides support for Fig. 2. This paragraph provides further specific information (size of gene (20 kb), number of exons (8), start (position 305 of exon 1) and stop (position 314 of exon 8) points of open reading frame, number of amino acids in

protein (571), number of transmembrane domains (9 or 10)) regarding the human SLC11A3 gene shown in Fig. 2. In this regard, paragraphs 62-64 provide yet further support regarding the specific features of the SLC11A3 gene shown in Fig. 2, especially with regard to the A-to-C transversion at position 734.

**Fig. 3:** Paragraph 47 on page 19 discloses that Fig. 3 shows a mutation analysis. This Figure is disclosed as a side-by-side analysis of sequences from a control and a patient having the heterozygous mutation depicted in the Figure.

Paragraph 83 on page 30 further provides support for Fig. 3. This paragraph describes the specific procedure used to test for the base change in exon 5 presented in Fig. 3. Further, this paragraph sets forth the specific sequences of both the normal (TATTGCA~~A~~ATTTGGC) and mutated (TATTGCACATTTGGC) sequences presented in Fig. 3. In this regard, paragraphs 63 and 64 provide a further description of the portion of the mutated SLC113A gene shown in Fig. 3.

**Fig. 4:** Paragraph 48 on page 19 discloses that Fig. 4 shows a sequence homology analysis of the region around the mutation. The indicators for the N144H amino acid substitution and the predicted transmembrane domains are

disclosed.

Paragraphs 64-65 on pages 25-26 further provide support for Fig. 4. These paragraphs describe the specific amino acid substitution at position 144 (N144H) caused by the mutation shown in Fig. 4. Further, these paragraphs disclose that due to the highly conserved nature of asparagine in vertebrates shown in Fig. 4, the substitution of asparagine suggests a pronounced effect on SLC11A3 function. Similarly, these paragraphs disclose that the mutation is important for metal ion binding since it resides within a region that otherwise shows little homology to SLC11A3, as shown in Fig. 4. Further, paragraphs 85-86 on page 31 disclose the specific procedures used to obtain the sequences shown in Fig. 4, providing further support for this Figure.

**Fig. 5:** Paragraph 49 on page 19 discloses that Fig. 5 shows the SLC11A3 expression via Northern blot in various human tissues. The types of human tissues and their locations in the Figure (left-adult human tissues, middle-human digestive tract, right-human monocytes and lymphoblast cells) are disclosed.

Paragraph 61 on page 24 further provides support for Fig. 5. This paragraph describes the findings of Fig. 5 that expression of SLC11A3 is highest in the digestive tract,

liver, placenta, kidneys, and monocytes. Similarly, paragraph 68 on page 27 provides support for Fig, 5, disclosing the reasons behind the accumulation of iron in blood plasma and body tissues shown by Fig. 5.

**Fig, 6:** Paragraph 50 on page 19 discloses that Fig. 6 shows a model for iron transport from the gut lumen throughout the body through enterocytes into the circulation and subsequent accumulation in the liver.

Paragraph 66 on page 26 further provides support for Fig. 6. This paragraph describes the specific iron transport model shown in Fig. 6, including that ferrous iron ( $\text{Fe}^{2+}$ ) is transported through the apical surface of the enterocytes by the divalent metal transporter (DMT1). This paragraph further discloses the showing in Fig. 6 that iron can then be stored as ferritin or transported across the basolateral membrane by SLC113A with the aid of Hephaestin. This paragraph also discloses the showing in Fig. 6 that, once it reaches the blood plasma, iron is then loaded onto ferrotransferrin (Tf) as ferric iron ( $\text{Fe}^{3+}$ ) and subsequently taken up by body tissues, such as the liver, by transport over a transferrin receptor (TFR) that is associated with HFE. Accordingly, the exact iron transport model of Fig. 6 is disclosed in paragraph 66.

Accordingly, entry of these Drawings into the present application is respectfully requested.

Claims 1, 2, 6, 7, and 27-32 are currently pending in the present application. The claims have been amended in the expectation that the amendments will place this application in condition for allowance. Claims 1, 6, and 29 have been amended as suggested by the Examiner to replace the phrase "SEQ ID NO. 1" with the phrase "SEQ ID NO: 1". The specification has similarly been amended in accordance with the Examiner's suggestions. Further, claims 1, 6, 27, and 29 have been amended to further clarify the invention in accordance with the Examiner's suggestions. The amendments do not introduce new matter within the meaning of 35 U.S.C. § 132. Accordingly, entry of the amendments is respectfully requested.

Applicants note the Examiner's statements regarding the Restriction Requirement that:

In the event that Claims 1-2, 6-7, 27-29 become directed to an allowable product, pursuant to the procedures set forth in the Official Gazette notice dated March 26, 1996 (1184 O.G. 86), claims 30-32, directed to the process of making or using the patentable product, previously withdrawn from consideration as a result of a restriction requirement would be considered for rejoinder. However, Claims 33-38 are not directed to the process of making or using the patentable product and will not be considered for rejoinder. Furthermore, Claim 3, as written, will not be considered for rejoinder because Claim 3 does not require the nucleic acid of Claim 1.

In view of the claim amendments above, the arguments presented

below, and the Examiner's indication that an "isolated nucleic acid of SEQ ID NO: 1 is free of the art" and is allowable subject matter, applicants hereby submit that claims 30-32 of the present application are suitable for rejoinder in accordance with the Examiner's statement above. Accordingly, these claims 30-32 are presented herein for the Examiner's consideration.

**1. Rejection of Claims 1-2, 6-7, and 29 under 35 U.S.C. § 112, 1st paragraph**

The Official Action states that claims 1-2, 6-7, and 29 are rejected under 35 U.S.C. § 112, first paragraph for the following reasons:

Claims 1-2, 6-7, and 29 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are broadly drawn to "an isolated DNA sequence up to 20 kb in length comprising a nucleic acid sequence as shown in SEQ ID NO: 1." Claim 29 is drawn to a partial sequence of SEQ ID NO: 1.

The phrase "as shown in SEQ ID NO: 1" has been broadly interpreted to mean any sequence shown in SEQ ID NO: 1 embedded within another isolated DNA sequence. For example, the claim encompasses any 10-mer of SEQ ID NO: 1 embedded within another sequence. Alternatively, a claim drawn to an isolated nucleic DNA sequence up to 20 kb in length comprising a nucleic acid sequence of SEQ ID NO: 1 would require a nucleic acid comprising all of SEQ ID NO: 1.

The specification teaches a single isolated DNA sequence within the scope of the claims. The nucleic acid sequence of SEQ ID NO: 1 comprises a single mutation in exon 5, namely a transversion at position 734 in exon 5. The art teaches a missense mutation converting alanine to

aspartic acid at residue 77 (A77D) which was not found in control individuals (Montosi et al. J. of Clinical Investigation, Vol. 108, No. 4, pages 619-623, August 2001)). The art also teaches several additional mutations within the ferroportin 1 gene (Devalia et al. Blood, Vol. 100, No. 2, pages 695-697, July 2002). These mutations include a variation in the promoter region of trinucleotide repeats, a G-C transversion within the first intron; a transversion in codon 221, a 3 base pair deletion in exon 5, for example (page 696, col. 1-2). *Vas-Cath Inc. V. Mahurkar*, 19USPQ2b 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. In *The Regents of the University of California v. Eli Lilly* (43 USPQ2b 1398-1412), the court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA..." required a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention". In analyzing whether the written description requirement is met for a genus claim, it is first determined whether a representative number of species have been described by their complete structure. In the instant case, the claims have defined only a fragment of a nucleic acid sequence. Based upon the interpretation of "shown in SEQ ID NO: 1" and "partial sequence" given to the claims, shown in, as stated above, encompasses any nucleic acid sequence "shown in SEQ ID NO: 1" or a "partial sequence of SEQ ID NO: 1" embedded within a larger sequence. In the broadest sense of the interpretation, any nucleic acid comprising an "A" is encompassed by the instant claims, as an "A" is shown in



SEQ ID NO: 1. Thus, the claims broadly read upon any number of genes which have not been described in addition to variant SLC11A3 genes not described. The claims broadly encompass nucleic acids which comprise any number of nucleotides of SEQ ID NO: 1 embedded within larger sequences. For example, the art teaches homo sapiens STS genomic which comprises over 130 nucleotides from SEQ ID NO: 1 (see Olivier, Genbank Accession Number G11389, March 20, 2000). The claims are written broadly enough to genomic and cDNA sequences which have not been described by the instant specification. Thus, the claims broadly encompasses a large genus of nucleic acid which have not been described within the instant specification. The claims also broadly encompass variant SLC11A3 genes. The art has not described a representative number of SLC11A3 genes. For example, the instant specification fails to describe the missense mutation converting alanine to aspartic acid at residue 77 (A77D) which was not found in control individuals (Montosi et al. J. of Clinical Investigation, Vol. 108, No. 4, pages 619-623, August 2001). The art also teaches several additional mutations within the ferroportin 1 gene (Devalia et al. Blood, Vol. 100, No. 2, pages 695-697, July 2002). These mutations include a variation in the promoter region of trinucleotide repeats, a G-C transversion within the first intron; a transversion in codon 221, a 3 base pair deletion in exon 5, for example (page 696, col. 1-2). Each of these variations are encompassed by the instant claims, however, were not described by the instant specification. The specification has also not defined a structural feature of the variants which would be common to all members of the genus that constitutes a substantial portion of the genus.

One of skill in the art would conclude that applicant was not in possession of the claimed "isolated DNA sequences comprising a nucleic acid sequence as shown in SEQ ID NO: 1" or a partial sequence of SEQ ID NO: 1" because the description of a single member of this genus is not representative of the variants of the genus and is insufficient to support the claims. Thus, the specification does not adequately provide a written description for "isolated DNA sequences comprising a nucleic acid sequence as shown in SEQ ID NO: 1" or a "partial sequence of SEQ ID NO: 1."

Applicants respectfully traverse this rejection. The test

under 35 U.S.C. 112, first paragraph, for determining compliance with the written description requirement is whether the application clearly conveys that an applicant has invented the subject matter which is claimed. *In re Barker*, 194 USPQ 470, 473 (CCPA 1977); MPEP 2163. Also, the applicant must convey to the public what the applicant claims as the invention so that the public may ascertain if the patent applicant claims anything in common use or already known. MPEP 2163. Lastly, the specification must convey that the applicant was in possession of the invention. MPEP 2163. The Examiner is respectfully reminded that the Examiner has the initial burden of presenting evidence or reasons why persons skilled in the art would not recognize in an applicant's disclosure a description of the invention defined by the claims. *In re Wertheim*, 191 USPQ 90, 98 (CCPA 1976).

Applicants thank the Examiner for her suggestions regarding the claims. Accordingly, applicants have amended claim 1 to relate to "a nucleic acid sequence that is SEQ ID NO: 1" rather than "a nucleic acid sequence as shown in SEQ ID NO: 1". Claim 1, then, clearly does not encompass any sequence shown in SEQ ID NO: 1, as suggested by the Examiner, but rather encompasses SEQ ID NO: 1 itself.

Similarly, applicants have amended claims 6 and 29 to relate to a sequence unique to SEQ ID NO: 1 "having a single nucleotide substitution of A-to-C at position 734 (A734C) in exon 5 of said

SEQ ID NO: 1 in comparison with non-mutated SLC11A3." Accordingly, the sequences encompassed by these claims must contain the novel "single mutation in exon 5, namely a transversion at position 734 in exon 5" noted by the Examiner. Claims 6 and 29, then, clearly only encompass sequences containing this novel mutation noted by the Examiner.

Accordingly, applicant respectfully requests the Examiner to reconsider and withdraw the rejection of pending claims 1-2, 6-7, and 29.

**2. Rejection of Claims 6-7 and 27-28 under 35 U.S.C. § 112, 2d paragraph**

The Official Action states that claims 6-7 and 27-28 are rejected under 35 U.S.C. § 112, second paragraph for the following reasons:

Claims 6-7, 27-28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regards as the invention.

A) Claims 6-7 are indefinite over the recitation "a sequence unique to SEQ ID NO: 1" because it is unclear what constitutes a sequence unique to SEQ ID NO: 1. Based upon the disclosure in the specification and the art, the art teaches SEQ ID NO: 1 with a single base pair transversion at position 734. Moreover, the art teaches numerous primers or oligonucleotides, including every possible 10-mer oligonucleotide. Therefore, it is unclear what constitutes a unique sequence. It is unclear whether the oligonucleotide must be unique in compared to the "wild-type" sequence or whether the at least 8 nucleotides must be from a sequence unique to SEQ ID NO: 1, but need not be unique themselves. For example, SEQ ID NO: 1 is unique to SEQ ID NO: 1, therefore, it is unclear whether any 8 consecutive

nucleotides from SEQ ID NO: 1 would fall within the scope of the claims. Thus, the metes and bounds of "a sequence unique to SEQ ID NO: 1" is unclear.

B) Claims 27-28 are indefinite over the recitation (A734C) because it is unclear whether this parenthetical is merely providing an example of a polymorphism at position 734.

Applicants respectfully traverse this rejection. Regarding the §112, second paragraph rejection, caselaw has defined two requirements under the statute: (1) whether the applicant has stated the invention as something elsewhere in the application which would not fall under the scope of the claims; and (2) whether the claims would be communicated with a reasonable degree of particularity and distinctness to a person skilled in the art in light of the content of the disclosure and the teachings of the prior art. MPEP §2171, §2173, and §2173.02.

Applicants thank the Examiner for her suggestions regarding the claims. Accordingly, applicants have amended claim 6 to specify that the "sequence unique to SEQ ID NO: 1" has "a single nucleotide substitution of A-to-C at position 734 (A734C) in exon 5 of said SEQ ID NO: 1 in comparison with non-mutated SLC11A3." Accordingly, claim 6 clearly only encompasses sequences containing this novel mutation.

Similarly, applicants have amended claim 27 to specify "an A-to-C" base mutation at position 734. Accordingly, it is clear that the recitation of "(A734C)" is parenthetical for the specific base mutation required by the claim.

Accordingly, applicants respectfully request the Examiner to

reconsider and withdraw the rejection of pending claims 6-7 and 27-28.

**3. Rejection of Claims 1-2, 6-7, and 29 under 35 U.S.C. § 102(b)**

The Official Action states that claims 1-2, 6-7, and 29 are rejected under 35 U.S.C. § 102(b) as being anticipated by McKie et al.

As the basis of this rejection, the Official Action states:

Claims 1-2, 6-7, 29 are rejected under 35 U.S.C. 102(b) as being anticipated by McKie et al. (Genbank Accession Number AF231121, March 2000).

McKie teaches the IREG1 complete cDNA comprising over 1,500 contiguous nucleotides from SEQ ID NO: 1 (limitations of Claim 2). The nucleic acid sequence of SEQ ID NO: 1 and McKie differ only at a single nucleotide, namely nucleotide 734. The nucleic acid of McKie is an isolated DNA sequence up to 20 kb in length comprising a nucleic acid shown in SEQ ID NO: 1. The nucleic acid shown in SEQ ID NO: 1 is nucleotides 735-2243 of McKie (limitations of Claim 1).

With respect to Claim 6-7, the nucleic acid is at least 8 consecutive nucleotides selected from SEQ ID NO: 1, namely nucleotides 1-733 are 100% identical. Claim 7 remains drawn to a single oligonucleotide. The limitations of Claim 7 do not add any structural limitations to the Claims, therefore, the nucleic acid of McKie anticipates the claim.

With respect to claim 29, McKie teaches a nucleic acid comprising a partial sequence of SEQ ID NO: 1, namely positions 735-2243. The nucleic acids of McKie may be used as a predictive marker for HH gene mutation. If the "normal" DNA hybridizes under high stringent conditions, this may be used in sequencing assays to predict that there is no HH gene mutation.

An isolated nucleic acid of SEQ ID NO: 1 is free of the art. The art does not teach cDNA from the SLC11A3 (SEQ ID NO: 1) containing a mutation in exon 5, position 734 which results in a transversion between an A-C. The instant specification states that "all symptomatic HH

patients contain a heterozygous A-to-C transversion at position 734 (A734C) compared to 200 healthy controls (page 25, para 63). The specification states that the base change is the causative mutation for HH.

Applicants respectfully traverse this rejection. The test for anticipation is whether each and every element as set forth is found, either expressly or inherently described, in a single prior art reference. *Verdegaal Bros. v. Union Oil Co. of California*, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987); MPEP §2131. The identical invention must be shown in as complete detail as is contained in the claim. *Richardson v. Suzuki Motor Co.*, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989); MPEP §2131. The elements must also be arranged as required by the claim. *In re Bond*, 15 USPQ2d 1566 (Fed. Cir. 1990).

Applicants thank the Examiner for her indication that an "isolated nucleic acid of SEQ ID NO: 1 is free of the art" and is allowable subject matter. Accordingly, applicants have amended claim 1 to relate to "a nucleic acid sequence that is SEQ ID NO: 1." Claim 1, then, is clearly not anticipated by the cited prior art and represents allowable subject matter, as confirmed by the Examiner.

Similarly, applicants have amended claims 6 and 29 to relate to a sequence unique to SEQ ID NO: 1 "having a single nucleotide substitution of A-to-C at position 734 (A734C) in exon 5 of said SEQ ID NO: 1 in comparison with non-mutated SLC11A3." Accordingly, the sequences encompassed by these claims must contain the novel "mutation in exon 5, position 734 which results in a transversion

between an A-C" noted by the Examiner. Claims 6-7 and 29, then, are clearly not anticipated by the cited prior art and represent allowable subject matter, as confirmed by the Examiner.

Accordingly, applicants respectfully request the Examiner to reconsider and withdraw the rejection of pending claims 1-2, 6-7, and 29.

**4. Rejection of Claims 1, 6-7, and 29 under 35 U.S.C. § 102(b)**

The Official Action states that claims 1, 6-7, and 29 are rejected under 35 U.S.C. § 102(b) as being anticipated by Olivier et al.

As the basis of this rejection, the Official Action states:

Claims 1, 6-7, 29 are rejected under 35 U.S.C. 102(b) as being anticipated by Olivier et al. (Genbank Accession Number G11389, March 2000).

Olivier et al. (herein referred to as Olivier) teaches a nucleic acid from human STS genomic sequence tagged site. The nucleic acid comprises over 130 contiguous nucleotides from the complement of SEQ ID NO: 1 (limitations of Claim 1). Positions 2036-2062 of SEQ ID NO :1 is 100% identical to positions 286-153 of Olivier. Olivier also teaches two primers, namely primer A and primer B which are located within SEQ ID NO: 1. These nucleic acids are 20 nucleotides in length. Therefore, each of these primers are at least 8 consecutive nucleotides from SEQ ID NO: 1 which are part of an oligonucleotide pair for amplification (limitations of Claims 6-7).

With respect to claim 29, the two primers, namely primer A and primer B comprise a partial sequence of SEQ ID NO: 1. These oligonucleotides would have the property of amplifying the gene, thus would be predictive of a HH gene mutation.

An isolated nucleic acid of SEQ ID NO: 1 is free of the art. The art does not teach cDNA from the SLC11A3 (SEQ

ID NO: 1) containing a mutation in exon 5, position 734 which results in a transversion between an A-C. The instant specification states that "all symptomatic HH patients contain a heterozygous A-to-C transversion at position 734 (A734C) compared to 200 healthy controls (page 25, para 63). The specification states that the base change is the causative mutation for HH.

Applicants respectfully traverse this rejection. The test for anticipation is whether each and every element as set forth is found, either expressly or inherently described, in a single prior art reference. *Verdegaal Bros. v. Union Oil Co. of California*, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987); MPEP §2131. The identical invention must be shown in as complete detail as is contained in the claim. *Richardson v. Suzuki Motor Co.*, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989); MPEP §2131. The elements must also be arranged as required by the claim. *In re Bond*, 15 USPQ2d 1566 (Fed. Cir. 1990).

Applicants thank the Examiner for her indication that an "isolated nucleic acid of SEQ ID NO: 1 is free of the art" and is allowable subject matter. Accordingly, applicants have amended claim 1 to relate to "a nucleic acid sequence that is SEQ ID NO: 1." Claim 1, then, is clearly not anticipated by the cited prior art and represents allowable subject matter, as confirmed by the Examiner.

Similarly, applicants have amended claims 6 and 29 to relate to a sequence unique to SEQ ID NO: 1 "having a single nucleotide substitution of A-to-C at position 734 (A734C) in exon 5 of said SEQ ID NO: 1 in comparison with non-mutated SLC11A3." Accordingly, the sequences encompassed by these claims must contain the novel



"mutation in exon 5, position 734 which results in a transversion between an A-C" noted by the Examiner. Claims 6-7 and 29, then, are clearly not anticipated by the cited prior art and represent allowable subject matter, as confirmed by the Examiner.

Accordingly, applicants respectfully request the Examiner to reconsider and withdraw the rejection of pending claims 1, 6-7, and 29.

**5. Rejection of Claims 1-2, 6-7, and 29 under 35 U.S.C. § 102(b)**

The Official Action states that claims 1-2, 6-7, and 29 are rejected under 35 U.S.C. § 102(b) as being anticipated by Brennan.

As the basis of this rejection, the Official Action states:

Claims 1-2, 6-7, 29 are rejected under 35 U.S.C. 102(b) as being anticipated by Brennan (US Patent 5,474,796, December 12, 1995).

The instant claims are drawn to an isolated DNA sequence comprising a nucleic acid shown in SEQ ID NO: 1. Shown in has been broadly interpreted to mean any fragment which is depicted in SEQ ID NO: 1. Thus, fragments of 10 nucleotides is encompassed within the claims.

Furthermore, "unique" has been broadly interpreted to mean any sequence which appears in SEQ ID NO: 1 for the reason provided in the 112/2<sup>nd</sup> rejection above.

Brennan teaches oligonucleotides having 10 nucleotides each (10-mers). The oligonucleotides represent every possible permutation of the 10-mer oligonucleotide. Therefore, Brennan teaches every possible 10-mer nucleic acid. The 10-mer oligonucleotides taught by Brennan represent every possible nucleic acid fragment from within SEQ ID NO: 1.

With respect to claim 2, the 10-mer nucleic acids synthesized by Brennan are DNA molecules. cDNA molecules are composed of DNA nucleotides, just as DNA molecules are composed of DNA nucleotides. The structure of cDNA is the same as DNA molecules. Thus, the same sequence is chemically identical. Therefore, the 10-mer molecules of

Brennan do not differ in structure from 10-mer cDNA molecules.

With respect to claim 29, the 10-mer nucleic acids of Brennan comprise a partial sequence of SEQ ID NO: 1. The oligonucleotides would minimally have the property of amplifying the gene, thus would be predictive of a HH gene mutation.

An isolated nucleic acid of SEQ ID NO: 1 is free of the art. The art does not teach cDNA from the SLC11A3 (SEQ ID NO: 1) containing a mutation in exon 5, position 734 which results in a transversion between an A-C. The instant specification states that "all symptomatic HH patients contain a heterozygous A-to-C transversion at position 734 (A734C) compared to 200 healthy controls (page 25, para 63). The specification states that the base change is the causative mutation for HH.

Applicants respectfully traverse this rejection. The test for anticipation is whether each and every element as set forth is found, either expressly or inherently described, in a single prior art reference. *Verdegaal Bros. v. Union Oil Co. of California*, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987); MPEP §2131. The identical invention must be shown in as complete detail as is contained in the claim. *Richardson v. Suzuki Motor Co.*, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989); MPEP §2131. The elements must also be arranged as required by the claim. *In re Bond*, 15 USPQ2d 1566 (Fed. Cir. 1990).

Applicants thank the Examiner for her indication that an "isolated nucleic acid of SEQ ID NO: 1 is free of the art" and is allowable subject matter. Accordingly, applicants have amended claim 1 to relate to "a nucleic acid sequence that is SEQ ID NO: 1." Claim 1, then, is clearly not anticipated by the cited prior art and represents allowable subject matter, as confirmed by the Examiner.

Similarly, applicants have amended claims 6 and 29 to relate to a sequence unique to SEQ ID NO: 1 "having a single nucleotide substitution of A-to-C at position 734 (A734C) in exon 5 of said SEQ ID NO: 1 in comparison with non-mutated SLC11A3." Accordingly, the sequences encompassed by these claims must contain the novel "mutation in exon 5, position 734 which results in a transversion between an A-C" noted by the Examiner. Claims 6-7 and 29, then, are clearly not anticipated by the cited prior art and represent allowable subject matter, as confirmed by the Examiner.

Accordingly, applicants respectfully request the Examiner to reconsider and withdraw the rejection of pending claims 1-2, 6-7, and 29.

**6. Rejection of Claims 27-28 under 35 U.S.C. § 102(b)**

The Official Action states that claims 27-28 are rejected under 35 U.S.C. § 102(b) as being anticipated by Boehringer Mannheim.

As the basis of this rejection, the Official Action states:

Claims 27-28 are rejected under 35 U.S.C. 102(b) as being anticipated by Boehringer Mannheim (1997 Biochemicals Catalog, page 95).

It is noted that these claims contain a preamble which recites an intended use, however, it is also noted that this use does not confer patentable weight on the product claims since the preamble does not materially change what is present in the kit itself and thus represents an intended use of the kit (see MPEP 2111.02).

Boehringer Mannheim teaches a kit comprising hybridization bags which can be used in non-radioactive hybridization and detection procedures. This is a kit as

minimally required by Claim 27. Moreover, the kit can be used for detecting the presence or absence of a base mutation in a hybridization or detection procedure. Also, Boehringer Mannheim teaches a hexanucleotide mix provided within a kit. The mixture of hexamer nucleotides comprises primers for amplifying DNA containing the base-pair polymorphism. Thus, the Boehringer Mannheim Catalog teaches a kit comprising primers for amplifying the DNA containing the base-pair polymorphism at position 734 of the SLC11A3 gene. An isolated nucleic acid of SEQ ID NO: 1 is free of the art. The art does not teach cDNA from the SLC11A3 (SEQ ID NO: 1) containing a mutation in exon 5, position 734 which results in a transversion between an A-C. The instant specification states that "all symptomatic HH patients contain a heterozygous A-to-C transversion at position 734 (A734C) compared to 200 healthy controls (page 25, para 63). The specification states that the base change is the causative mutation for HH.

Applicants respectfully traverse this rejection. The test for anticipation is whether each and every element as set forth is found, either expressly or inherently described, in a single prior art reference. *Verdegaal Bros. v. Union Oil Co. of California*, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987); MPEP §2131. The identical invention must be shown in as complete detail as is contained in the claim. *Richardson v. Suzuki Motor Co.*, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989); MPEP §2131. The elements must also be arranged as required by the claim. *In re Bond*, 15 USPQ2d 1566 (Fed. Cir. 1990).

Applicants thank the Examiner for her suggestions regarding the claims. Accordingly, applicants have amended claim 27 to specify that the claimed kits comprise "an antibody which specifically binds to a gene product of the mutated SLC11A3 gene in

combination with a reagent for detecting binding of the antibody to the gene product". In contrast, Boehringer Mannheim does not teach or suggest kits containing an antibody that specifically binds to the specifically recited gene product of the mutated SLC11A3 gene, i.e. a gene product having an A-to-C base mutation at position 734 (A734C) of the SLC11A3 gene. Boehringer Mannheim, then, does not teach each and every element as set forth in the claims, as required by *Verdegaal Bros. v. Union Oil Co. of California*.

Accordingly, applicants respectfully request the Examiner to reconsider and withdraw the rejection of pending claims 27-28.

#### **CONCLUSION**

Based upon the above amendments and remarks, the presently claimed subject matter is believed to be novel and patentably distinguishable over the prior art of record. The Examiner is therefore respectfully requested to reconsider and withdraw the rejections of pending claims 1-2, 6-7, and 27-32. Favorable action with an early allowance of the claims pending in this application is earnestly solicited.


The Examiner is welcomed to telephone the undersigned attorney  
if she has any questions or comments.

Respectfully submitted,

**NATH & ASSOCIATES PLLC**

Date: 23 Oct. 2003

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